REMARKS

I. Status Summary

Claims 1-13 and 15-17 are pending and have been examined by the United States Patent and Trademark Office (hereinafter "the Patent Office") in a Non-Final Official Action dated March 6, 2008 (hereinafter "the Non-Final Official Action").

Claim 1 has been subjected to an objection.

Claims 1-9 have been rejected under the enablement provision of 35 U.S.C. 112, first paragraph.

Claim 8 has been rejected under 35 U.S.C. 112, second paragraph, upon the contention that the claim is indefinite.

Claims 1-10, 12, and 13 have been rejected under 35 U.S.C. 102(e) upon the contention that the claims are anticipated by U.S. Patent No. 6,777,439 to Durden (hereinafter "Durden"). Claims 1-9 and 15 have also been rejected under 35 U.S.C. 102(a) upon the contention that the claims are anticipated by National Cancer Institute (Clinical Trials), first published September 1, 2001 (hereinafter "NCI Clinical Trials"). Claims 1-7 and 15 have also been rejected under 35 U.S.C. 102(b) upon the contention that the claims are anticipated by Laird *et al.* (2000) *Cancer Res* 60:4152-4160 (hereinafter "Laird").

Claims 1-13 and 17 have been rejected under 35 U.S.C. 103(a) upon the contention that the claims are unpatentable over Durden taken with Walker *et al.* (2000) *Molecular Cell* 6:909-919, in view of U.S. Patent No. 6,025,365 to Weichselbaum et al. (hereinafter "Weichselbaum"). Claims 1, 15, and 16 have also been rejected under 35 U.S.C. 103(a) upon the contention that the claims are unpatentable over Durden in view of Ning *et al.* (2001) *Radiation Research* 157:45-51 (hereinafter "Ning"), NCI Clinical Trials, and further in view of U.S. Patent No. 6,573,293 to Tang et al. (hereinafter "Tang").

Claim 5 has been canceled without prejudice. Applicants hereby reserve the right to file one or more continuing applications with claims directed to the subject matter of the canceled claim.

Claims 1, 4, and 6 have been amended. Support for the amendments can be found throughout the specification as filed, including particularly at page 3, line 4.

Additional support can be found on page 8, lines 24-26 and in claims 2 and 4-6 as filed. Thus, no new matter has been added by the amendments to claims 1, 4, and 6.

Reconsideration of the application as amended and based on the remarks presented hereinbelow is respectfully requested.

II. Response to the Claim Objection

Claim 1 has been subjected to an objection. Particularly, the Patent Office asserts that the abbreviation "PI3K" should be spelled out the first time it is used in the claims.

Applicants have amended claim 1 in accordance with the Patent Office's suggestion. Applicants respectfully submit that the amendment to claim 1 addresses the instant objection, and respectfully request that it be withdrawn at this time.

III. Response to the Enablement Rejection

Claims 1-9 have been rejected under the enablement provision of 35 U.S.C. § 112, first paragraph. According to the Patent Office, the specification enables increasing the radiosensitivity of a target tissue in a subject comprising administering a phosphatidylinositol 3-kinase (PI3K) antagonist to the subject when the PI3K antagonist is selected from among LY294002, Wortmannin, SU6668, SU11248 and Genistein, but does not reasonably provide enablement for the administration of other PI3K antagonists to a target tissue in a subject.

After careful consideration, applicants respectfully traverse the rejection and the Patent Office's comments and offer the following remarks.

Initially, applicants respectfully submit that, as described hereinabove, claim 5 has been canceled. Thus, the rejection of claim 5 has been rendered moot.

Applicants respectfully submit that with regard to whether the enablement is commensurate with the scope of the claims, "the specification must teach those skilled in the art how to make and use the full scope of the claimed invention without 'undue experimentation'." See Manual of Patent Examining Procedure (hereinafter "MPEP") § 2164.08, citing *In re Wright*, 999 F.2d 1557, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993). The scope of enablement must only bear a "reasonable correlation" to the scope of the

claims. Id., citing *In re Fisher* 427, F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1070). In particular, "how a teaching is set forth, by specific example or broad terminology, is not important." Id., citing *In re Marzocchi*, 439, F.2d 220, 223-24 169 USPQ 367, 370 (CCPA 1971); emphasis added. Further, that some experimentation may be necessary, and may be complex, does not make it undue if it is no more complex than that typically engaged in the art. See MPEP § 2164.01. See also, *In re Certain Limited-Charge Cell Culture Microcarriers*, 221, USPQ 1165, 1174 (Int'l Trade Comm'n 1983), *aff'd. sub. nom., Massachusetts Institute of Technology v. A. B. Fortia*, 774 F. 2d 1104, 227 USPQ 428 (Fed. Cir. 1985) and *In re Angstadt*, 537 F.2d 498, 504, 190 USPQ 214, 219 (CCPA 1976).

Applicants respectfully submit that the instant specification as filed recites that a PI3K antagonist is a molecule or other chemical entity having a capacity for specifically binding to PI3K to inhibit a PI3K activity. See Instant Specification, page 12, lines 27-29. The instant specification further defines PI3K antagonist as a molecule or other chemical entity that has the capacity for preventing Akt activation, including broad spectrum receptor tyrosine kinase inhibitors that prevent radiation induced activation of the PI3K/AKt signaling pathway. See Instant Specification, page 12, line 29 to page 13, line 4. The instant specification describes that such molecules and chemical entities include small molecule inhibitors, neutralizing antibodies, and soluble PI3K polypeptides. See Instant Specification, page 13, lines 4-6. Target binding affinities of the inhibitors for their target (i.e., PI3K) are described in the instant specification at page 13, lines 10-12. Guidance regarding small molecules inhibitors are described in the instant specification at page 13, line 14 to page 14, line 4. Guidance regarding soluble PI3K polypeptides is provided in the instant specification at page 14, line 6 to page 26, line 8. Guidance regarding PI3K antibodies (i.e., antibodies that specifically bind to PI3K) is provided in the instant specification at page 26, line 9 to page 27, line 6.

In addition, applicants respectfully submit that the instant specification provides working examples showing that several small molecule PI3K antagonists of varying structure enhance the radiosensitivity of tumors, including radiation resistant tumors such as glioblastomas, and show that this activity appears to be related to the ability of the PI3K antagonists to prevent radiation-induced activation of the PI3K/Akt signaling

pathway. See for example, Instant Specification, page 51, lines 22-30. See also, Instant Specification, Example 3, page 42, line 10 to page 43, line 15 (with regard to the enhancement of radiation induced apoptosis using Wortmannin and LY294002); and Instant Specification, Example 14, page 52, line 24 to page 54, line 20 (with regard to the effect of SU11248 on radioresistance in GL261 glioblastomas).

Thus, applicants respectfully submit that the instant specification provides enablement with regard to the use of PI3K antagonists generally in methods of enhancing radiosensitivity of radiation resistant tumors.

Accordingly, applicants respectfully submit that the instant rejection has been addressed. Claim 5 has been canceled without prejudice, and thus the instant rejection is believed to be moot as to this claim. Therefore, applicants respectfully request that the instant rejection of claims 1-4 and 6-9 under the enablement provision of 35 U.S.C. § 112, first paragraph, be withdrawn, and further ask that claims 1-4 and 6-9 be allowed at this time.

IV. Response to the Rejection under 35 U.S.C. § 112, Second Paragraph

Claim 8 has been rejected under 35 U.S.C. § 112, second paragraph, upon the contention that the claim is indefinite. According to the Patent Office, it is not clear what the lower limit is for "a minimally therapeutic dose".

Applicants respectfully submit that the instant specification as filed defines "minimally therapeutic dose" as "the smallest dose, or smallest range of doses, determined to be a therapeutically effective amount" (see Instant Specification, page 37, lines 2-5). The instant specification also defines "therapeutically effective amount" as "an amount of a composition comprising a PI3K antagonist sufficient to produce a measurable anti-tumor response (e.g., an anti-angiogenic response, a cytotoxic response, and/or tumor regression)" (see Instant Specification, page 36, lines 19-22). Therefore, applicants respectfully submit that one of ordinary skill in the art would understand that a "minimally therapeutic dose" would be the smallest dose or smallest range of doses of a composition comprising a PI3K antagonist sufficient to produce a measurable anti-tumor response (e.g., an anti-angiogenic response, a cytotoxic response, and/or tumor regression)". Given that claim terminology meets the

requirements of 35 U.S.C. § 112, second paragraph if the meaning of the claim terminology is "discernable" by one of ordinary skill in the art (see MPEP § 2173.02), applicants respectfully submit that the claim 8 is believed to comply with the requirements of 35 U.S.C. § 112, second paragraph.

Additionally, applicants respectfully submit that the MPEP also states:

> A fundamental principle contained in 35 U.S.C. 112, second paragraph is that applicants are their own lexicographers. They can define in the claims what they regard as their invention essentially in whatever terms they choose so long as any special meaning assigned to a term is clearly set forth in the specification. See MPEP § 2111.01. Applicant may use functional language, alternative expressions, negative limitations, or any style of expression or format of claim which makes clear the boundaries of the subject matter for which protection is sought.

See MPEP § 2173.02 (emphasis added). Applicants respectfully submit that with respect to claim 8, the functional language "minimally therapeutic dose" has been employed because the compositions to which this phrase refers, the "PI3K antagonists", can be small molecule inhibitors, neutralizing antibodies, soluble PI3K polypeptides, and dominant negative PI3K polypeptides, among others. Applicants respectfully submit that a single unit of measure would not necessarily be applicable to all of these molecules to establish a single "lower limit", not least because these antagonists might be expected to have differing biological activities per unit mass, for example. Therefore, functional language was chosen to express this element recited in claim 8.

Accordingly, since functional language is clearly permitted in the claims as set forth in MPEP § 2173.02 and the language employed in claim 8 would be understood by one of ordinary skill in the art, applicants respectfully submit that claim 8 fully complies with the requirements of 35 U.S.C. § 112, second paragraph. As a result, applicants respectfully request that the instant rejection of claim 8 be withdrawn at this time.

V. Responses to the Rejections under 35 U.S.C. § 102

Claims 1-10, 12, and 13 have been rejected under 35 U.S.C. § 102(e) upon the contention that the claims are anticipated by Durden. Claims 1-9 and 15 have been rejected under 35 U.S.C. § 102(a) upon the contention that the claims are anticipated by

NCI Clinical Trials. Claims 1-7 and 15 have also been rejected under 35 U.S.C. § 102(b) upon the contention that the claims are anticipated by Laird.

After careful consideration of the rejection and the Patent Office's basis therefor, applicants respectfully traverse the rejections and submit the following remarks.

V.A. Response to the Rejection over Durden

Claims 1-10, 12, and 13 have been rejected under 35 U.S.C. § 102(e) upon the contention that the claims are anticipated by Durden. According to the Patent Office, Durden discloses regulating p53 mediated gene expression by administering PI3K inhibitors to increase chemosensitivity/radiosensitivity of tumor cells (brain tumors), wherein the PI3K antagonist is LY294002 or Wortmannin. The reference is also asserted to teach the LY294002 was administered at 100 mg/kg, wherein the subject is a mammal (mice), that the target tissue to be a vascular endothelial tumor (brain), wherein the target tissue is a vasculature supplying blood flow, that the PI3K regulates the proliferation of new blood supply, and that the PI3K antagonist is administered in a pharmaceutical carrier.

Applicants respectfully submit that claim 1 has been amended herein to recite a method of increasing the radiosensitivity of a radiation resistant tumor, wherein the method comprises providing a subject comprising a radiation resistant tumor and a target tissue, wherein the target tissue is selected from the group consisting of the radiation resistant tumor, endothelial tissue, and vasculature supplying blood flow to the radiation resistant tumor; and administering a phosphatidylinositol 3-kinase (PI3K) antagonist to the subject whereby the radiosensitivity of the radiation resistant tumor is increased. Support for the amendment can be found in the instant specification as filed at page 3, line 4. Additional support can be found on page 8, lines 24-26 and in claims 2 and 4-6 as filed.

In view of the amendment to claim 1, and as noted hereinabove, claim 5 has been canceled. Accordingly, the rejection of claim 5 has been rendered moot.

Further in view of the amendment to claim 1, claims 4 and 6 have been amended to recite "the radiation resistant tumor." Support for the amendment to claims 4 and 6 can be found in claim 5 as filed.

Applicants respectfully submit that claim 1 thus recites *inter alia* a method for increasing the radiosensitivity of a radiation resistant tumor. As conceded by the Patent Office, Durden fails to teach treatment of a radiation resistant tumor. See Official Action, page 10.

Accordingly, applicants respectfully request that the rejection of claims 1-4, 6-10, 12, and 13 under 35 U.S.C. § 102(e) over Durden be withdrawn, and further ask that claims 1-4, 6-10, 12, and 13 be allowed at this time.

V.B. Response to the Rejection over NCI Clinical Trials

Claim 1-9 and 15 have been rejected under 35 U.S.C. § 102(a) as allegedly being anticipated by NCI Clinical Trials. The Patent Office contends that NCI Clinical Trials teaches administering SU6668 to patients with solid tumors. The Patent Office further contends that solid tumors are resistant to radiation as evidenced by Vaupel et al., (*Medical Oncology*, 18(4), 2001, Abstract; hereinafter "Vaupel"). The Patent Office also contends that administration of SU6668 will target tissues such as endothelial tissues and vascular tissues.

As noted hereinabove, claim 1 has been amended herein to recite a method of increasing the radiosensitivity of a radiation resistant tumor, wherein the method comprises providing a subject comprising a radiation resistant tumor and a target tissue, wherein the target tissue is selected from the group consisting of the radiation resistant tumor, endothelial tissue, and vasculature supplying blood flow to the radiation resistant tumor; and administering a phosphatidylinositol 3-kinase (PI3K) antagonist to the subject whereby the radiosensitivity of the radiation resistant tumor is increased. Support for the amendment can be found in the instant specification as filed at page 3, line 4. Additional support can be found on page 8, lines 24-26 and in claims 2 and 4-6 as filed.

In view of the amendment to claim 1, claim 5 has been canceled. Accordingly, the rejection of claim 5 has been rendered moot. Further in view of the amendment to claim 1, claims 4 and 6 have been amended to recite "the radiation resistant tumor." Support for the amendment to claims 4 and 6 can be found in claim 5 as filed.

Applicants respectfully submit that claim 1 recites a method for increasing the radiosensitivity of a radiation resistant tumor. Applicants respectfully submit that NCI

Clinical Trials does not appear to teach a method involving increasing the radiosensitivity of a radiation resistant tumor.

With regard to the Patent Office's remarks concerning Vaupel, applicants respectfully submit that the Patent Office appears to be relying on Vaupel as evidence to show that a characteristic (i.e., the radiation resistance of solid tumors) not disclosed by NCI Clinical Trials is inherent. See MPEP § 2131.01. Applicants respectfully submit that, contrary to the Patent Office's apparent assertion, Vaupel does not appear to suggest that all solid tumors are necessarily radiation resistant. Applicants further respectfully submit that the "fact that a certain result or characteristic may occur ... is not sufficient to establish the inherency of that result or characteristic." See MPEP § 2112, citing *In re Rijckaert*, 9 F.3d 1531, 1534, 28 USPQ2d 1955, 1957 (Fed. Cir. 1993). Further:

> To establish inherency, the intrinsic evidence 'must make clear that the missing descriptive matter is necessarily present in the thing described in the reference, and that it would be so recognized by persons of ordinary skill. Inherency, however, may not be established by probabilities or possibilities. The mere fact that a certain thing may result from a given set of circumstances is not sufficient'" (emphasis added).

See MPEP § 2112, citing *In re Robertson*, 169 F.3d 743, 745, 49 USPQ2d 1949, 1950-51 (Fed. Cir. 1999).

Accordingly, applicants respectfully submit that NCI Clinical Trials as evidenced by Vaupel fails to support a rejection of claims 1-9 and 15 because NCI Clinical Trials does not necessarily disclose treatment of a radiation resistant tumor as recited in instant claim 1. Claims 2-4, 6-9 and 15 all depend from claim 1, and thus are also believed to be distinguished. Applicants respectfully request that the rejection of claims 1-4, 6-9 and 15 under 35 U.S.C. § 102(a) over NCI Clinical Trials be withdrawn, and further ask that claims 1-4, 6-9, and 15 be allowed at this time.

V.C. Response to the Rejection over Laird

Claim 1-7 and 15 have been rejected under 35 U.S.C. § 102(b) as allegedly being anticipated by Laird. The Patent Office alleges that Laird teaches that vascular endothelial growth factor is associated with solid tissue and SU6668 as a novel inhibitor of solid tumors. The Patent Office further alleges that increased radiosensitivity would

be an inherent property of SU6668 and that as clinical trials involve the administration of SU6668 as a pharmaceutical, it follows that SU6668 is in a pharmaceutical composition.

As noted hereinabove, claim 1 has been amended herein to recite a method of increasing the radiosensitivity of a radiation resistant tumor, wherein the method comprises providing a subject comprising a radiation resistant tumor and a target tissue, wherein the target tissue is selected from the group consisting of the radiation resistant tumor, endothelial tissue, and vasculature supplying blood flow to the radiation resistant tumor; and administering a phosphatidylinositol 3-kinase (PI3K) antagonist to the subject whereby the radiosensitivity of the radiation resistant tumor is increased. Support for the amendment can be found in the instant specification as filed at page 3, line 4. Additional support can be found on page 8, lines 24-26 and in claims 2 and 4-6 as filed.

In view of the amendment to claim 1, claim 5 has been canceled. Accordingly, the rejection of claim 5 has been rendered moot. Further in view of the amendment to claim 1, claims 4 and 6 have been amended to recite "the radiation resistant tumor." Support for the amendment to claims 4 and 6 can be found in claim 5 as filed.

Applicants respectfully submit that Laird does not describe the administration of SU6668 or any other PI3K antagonist in a method of increasing radiosensitivity of a radiation resistant tumor. At best, Laird describes the treatment of solid tumors. As described hereinabove, with regard to NCI Clinical Trials and Vaupel, the Patent Office has not supplied sufficient proof that all solid tumors are necessarily radiation resistant.

Therefore, applicants respectfully submit that Laird does not support a rejection of claim 1 under 35 U.S.C. § 102(b). Claims 2-4, 6, 7, and 15 all depend from claim 1, and thus are also believed to be distinguished over Laird. Accordingly, applicants respectfully request the withdrawal of the rejection of claims 1-4, 6, 7, and 15 under 35 U.S.C. § 102(b) over Laird and further ask that claims 1-4, 6, 7, and 15 be allowed at this time.

VI. Responses to the Rejections under 35 U.S.C. § 103(a)

Claims 1-13 and 17 have been rejected under 35 U.S.C. 103(a) upon the contention that the claims are unpatentable over Durden taken with Walker *et al.* (2000)

Molecular Cell 6:909-919, in view of U.S. Patent No. 6,025,365 to Weichselbaum et al. (hereinafter "Weichselbaum"). Claims 1, 15, and 16 have also been rejected under 35 U.S.C. 103(a) upon the contention that the claims are unpatentable over Durden in view of Ning *et al.* (2001) *Radiation Research* 157:45-51 (hereinafter "Ning") NCI Clinical Trials, and further in view of U.S. Patent No. 6,573,293 to Tang et al. (hereinafter "Tang").

After careful consideration of the rejection and the Patent Office's basis therefor, applicants respectfully traverse the rejections and submit the following remarks.

VI.A. Response to the Rejection over Durden and Walker in view of Weichselbaum

Claim 1-13 and 17 have been rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over Durden taken with Walker in view of Weichselbaum. The Patent Office contends that Durden teaches administering Wortmannin at concentrations of 10, 5, and 1 μg/mL but concedes that Durden fails to specifically teach administration to a radiation resistant tumor, use of SU6668 and SU11248, or use of a pharmaceutical carrier. The Patent Office alleges that Walker teaches that LY294002, Wortmannin, and Genistein are all PI3K inhibitors, and that it would be expected that the functions of these agents would be to increase radiosensitivity absent factual evidence. Finally, the Patent Office contends that Weichselbaum teaches that glioblastoma is a radiation resistant tumor.

As noted hereinabove, claim 1 has been amended herein to recite a method of increasing the radiosensitivity of a radiation resistant tumor, wherein the method comprises providing a subject comprising a radiation resistant tumor and a target tissue, wherein the target tissue is selected from the group consisting of the radiation resistant tumor, endothelial tissue, and vasculature supplying blood flow to the radiation resistant tumor; and administering a phosphatidylinositol 3-kinase (PI3K) antagonist to the subject whereby the radiosensitivity of the radiation resistant tumor is increased. Support for the amendment can be found in the instant specification as filed at page 3, line 4. Additional support can be found on page 8, lines 24-26 and in claims 2 and 4-6 as filed.

In view of the amendment to claim 1, claim 5 has been canceled. Accordingly, the rejection of claim 5 has been rendered moot. Further in view of the amendment to

claim 1, claims 4 and 6 have been amended to recite "the radiation resistant tumor." Support for the amendment to claims 4 and 6 can be found in claim 5 as filed.

Applicants respectfully submit that to support a rejection under 35 U.S.C. § 103, the Patent Office must demonstrate that the asserted references (a) teach or suggest all of the elements of a rejected claim; and (b) provide a finding that there was reasonable expectation of success. See MPEP § 2143. Applicants respectfully submit that Weichselbaum appears to describe the use of chelerythrine. Applicants respectfully submit that chelerythrine is a protein kinase C inhibitor (see Weichselbaum, column 8, line 66), not a PI3K inhibitor.

Accordingly, applicants respectfully submit that the use of chelerythrine in Weichselbaum would not provide one of ordinary skill in the art with a reasonable expectation of success in using a PI3K inhibitor in increasing the radiosensitivity of a radiation resistant tumor as recited in instant claim 1. Further, applicants respectfully submit that as Weichselbaum does not relate to the use of a PI3K inhibitor, there would be no motivation to combine Weichselbaum with Durden and Walker.

Therefore, applicants respectfully submit that Durden, Walker, and Weichselbaum, alone or in combination, do not support a rejection of claim 1 under 35 U.S.C. § 103(a). Claims 2-4, 6-13 and 17 all depend from claim 1, and thus are also believed to be distinguished over the cited combination.

Accordingly, applicants respectfully request that the rejection of claims 1-4, 6-13 and 17 under 35 U.S.C. § 103(a) over Durden, Walker, and Weichselbaum be withdrawn and further ask that claims 1-4, 6-13, and 17 be allowed at this time.

VI.B. Response to the Rejection over Durden in view of Ning and NCI Cancer Trials in further view of Tang

Claim 1 and 15-16 have been rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over Durden in view of Ning and NCI Cancer Trials in further view of Tang. The Patent Office alleges that Durden teaches regulating p53 mediated gene expression by administering PI3K inhibitors (i.e., LY294002) to increase chemosensitivity/radiosensitivity in tumor cells. The Patent Office further alleges that Ning teaches using SU6668 to enhance the efficacy of radiation therapy in mice bearing carcinomas and that NCI Cancer Trials teach administering SU6668 to solid tumors.

Further, the Patent Office alleges that Tang teaches pyrrole-substituted 2-indole compounds, including SU11248, that modulate the activity of protein kinase disorders. The Patent Office contends that one of ordinary skill in the art would have been motivated to use any tyrosine kinase inhibitor to enhance the radiosensitivity of a targeted tissue because abnormal growth activities have been related to protein tyrosine kinase, especially in brain cancer. The Patent Office also contends that, based on the multitarget aspect of the tyrosine inhibitor one of ordinary skill in the art would have been motivated to administer any of the claimed drugs and expect success in doing so.

As noted hereinabove, claim 1 has been amended herein to recite a method of increasing the radiosensitivity of a radiation resistant tumor, wherein the method comprises providing a subject comprising a radiation resistant tumor and a target tissue, wherein the target tissue is selected from the group consisting of the radiation resistant tumor, endothelial tissue, and vasculature supplying blood flow to the radiation resistant tumor; and administering a phosphatidylinositol 3-kinase (PI3K) antagonist to the subject whereby the radiosensitivity of the radiation resistant tumor is increased. Support for the amendment can be found in the instant specification as filed at page 3, line 4. Additional support can be found on page 8, lines 24-26 and in claims 2 and 4-6 as filed.

As noted further noted hereinabove, applicants respectfully submit that to support a rejection under 35 U.S.C. § 103, the Patent Office must demonstrate that the asserted references (a) teach or suggest all of the elements of a rejected claim; and (b) provide a finding that there was reasonable expectation of success. See MPEP § 2143.

As noted in Ning, there have been historical concerns that inhibition of tumor angiogenesis (e.g., by the administration of SU6668) might increase the hypoxic fraction of tumors and decrease the relative radiosensitivity of tumor cells. See Ning, page 49, right-hand column, last paragraph. Accordingly, applicants respectfully submit that the combination of Durden, Ning, NCI Cancer Trials, and Tang provides one of skill in the art with no reasonable expectation of success in increasing the radiosensitivity of a radiation resistant tumor as recited in claim 1. Claims 15 and 16 depend from claim 1, and thus are also believed to be distinguished over the cited combination.

Applicants respectfully request that the rejection of claims 1, 15 and 16 under 35 U.S.C. § 103(a) over Durden in view of Ning and NCI Cancer Trials in further view of Tang be withdrawn and further ask that claims 1, 15, and 16 be allowed at this time.

CONCLUSIONS

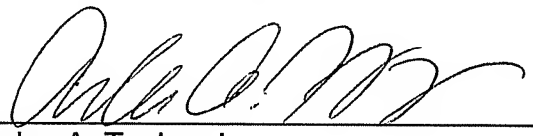
In light of the above amendments and remarks, it is respectfully submitted that the present application is now in proper condition for allowance, and an early notice to such effect is earnestly solicited.

If any small matter should remain outstanding after the Patent Examiner has had an opportunity to review the above Remarks, the Patent Examiner is respectfully requested to telephone the undersigned patent attorney in order to resolve these matters and avoid the issuance of another Official Action.

Deposit Account

The Commissioner is hereby authorized to charge any fees associated with the filing of this correspondence to Deposit Account Number **50-0426**.

Respectfully submitted,
JENKINS, WILSON, TAYLOR & HUNT, P.A.

Date: December 8, 2008 By: 

Arles A. Taylor, Jr.
Registration No. 39,395
Customer No. 25297
(919) 493-8000

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